REMARKS

Claims 21-38 are pending in the application and have been examined. The Examiner's allowance of Claims 22-27 is noted with appreciation. Claims 21, 28, 32, and 36-38 stand rejected and Claims 29-31 and 33-35 are objected to. Claims 36-38 have been canceled and Claim 21 has been amended. No new matter has been added. Applicants respectfully request reconsideration and allowance of Claims 21-35.

The Rejection of Claims 36-38 Under 35 U.S.C. § 102(b)

Claims 36-38 stand rejected under 35 U.S.C. § 102(b) as anticipated by EP 339285 or U.S. Patent No. 5,591,633. Applicants have canceled Claims 36-38 obviating this rejection.

The Rejection of Claims 21, 28, and 32 Under 35 U.S.C. § 103

Claims 21, 28, and 32 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 5,968,477 (Kasina et al.) in view of Giblin et al. (1997) *Bioconjugate Chem.* 8:347. Applicants respectfully traverse the rejection for the following reasons.

To more clearly define the invention, Claim 21 has been amended to recite that the modified annexin has an N-terminal chelation site comprising the amino acid sequence X_1-Gly-X_2, wherein X_1 and X_2 are selected from Gly and Cys, and wherein at least one of X_1 or X_2 is Cys. Support for the amendment can be found throughout the specification as originally filed, for example, at page 4, lines 17-21. Kasina et al. describes a conjugate having three distinct components: (1) a modified annexin, (2) a hexose moiety, and (3) a N_xS_y chelating compound. In contrast, the claimed invention is directed to isolated nucleic acid molecules and vectors encoding a polypeptide that bears no structural similarity to the conjugate described in Kasina et al. and host cells comprising these vectors. In contrast to the conjugate described by Kasina et al., the claimed invention does not include a sugar moiety, an N_xS_y chelating compound, or a sulfhydryl group provided for the purpose of conjugate formation. Furthermore,

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Kasina et al. fails to describe a modified annexin having an N-terminal amino acid extension that includes an amino acid sequence X_1-Gly-X_2, wherein X_1 and X_2 are selected from Gly and Cys, and wherein at least one of X_1 or X_2 is Cys, as in the claimed invention.

For the reasons noted above, the Kasina reference fails to teach, remotely suggest, provide any motivation to make, or otherwise render obvious the claimed invention.

The deficiencies of the teachings of the Kasina reference are not cured by the teachings of Giblin et al. Giblin et al. describes a modified alpha-melanotropin that includes an N-acetyl-Cys-Gly-Cys-Gly moiety. The reference provides no teaching, suggestion, or motivation to make a nucleic acid molecule encoding a modified annexin as in the claimed invention. Nor does the reference describe the three amino acid extensions of the claimed invention. Furthermore, applicants submit that one skilled in the art working on melanotropin analogs would not likely be aware of the clinical usefulness of annexins nor the site at which an annexin could be modified to avoid destroying its bioactivity. Therefore, Giblin et al. fails to suggest the claimed invention.

Because the cited references, either alone or in combination, fail to teach, suggest, provide motivation to make, or otherwise render obvious the claimed invention, applicants submit that the claimed invention is nonobvious and patentable over the cited references. Withdrawal of this rejection is respectfully requested.

The Rejection of Claims 21, 28, and 32 Under 35 U.S.C. § 103

Claims 21, 28, and 32 stand rejected under 35 U.S.C. § 103 as being unpatentable over Kasina et al., in view of U.S. Patent No. 5,849,261 (Dean et al.). Applicants respectfully traverse the rejection for the following reasons.

Claim 21 has been amended to recite that the modified annexin has an N-terminal chelation site comprising an amino acid sequence X_1-Gly-X_2, wherein X_1 and X_2 are selected

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from Gly and Cys, and wherein at least one of X_1 or X_2 is Cys. For the reasons noted above, Kasina et al. fails to teach, remotely suggest, provide any motivation to make, or otherwise render obvious the claimed invention.

The deficiencies of the teachings of Kasina et al. are not cured by the teachings of Dean et al. Dean et al. describes modified VIP peptides that include Gly-Gly-Cys and Cys-Gly-Gly moieties. Dean et al. provides no teaching, suggestion, or motivation to modify an annexin to include such a moiety. Furthermore, applicants submit that one skilled in the art working on VIP peptide analogs would not likely be aware of the clinical usefulness of annexins nor the site at which an annexin could be modified to avoid destroying its bioactivity. Therefore, Dean et al. fails to suggest the claimed invention.

Because the cited references, either alone or in combination, fail to teach, suggest, provide motivation to make, or otherwise render obvious the claimed invention, applicants submit that the claimed invention is nonobvious and patentable over the cited references. Withdrawal of this rejection is respectfully requested.

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CONCLUSION

In view of the above amendments and foregoing remarks, applicants believe that Claims 21-35 are in condition for allowance. If any issues remain that may be expeditiously addressed in a telephone interview, the Examiner is encouraged to telephone the applicants' attorney at 206.695.1755.

Respectfully submitted,

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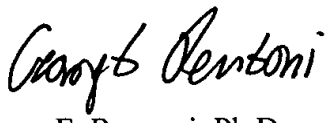

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